REMARKS

Telephone Interview

Applicants would like to express their appreciation to Examiner Lucas for the courtesy extended to Angela Dallas Sebor, Gladys Monroy, Richard Duke, and Tim Rodell during the telephone interview of December 14, 2005. During the interview, the rejections under 35 U.S.C. § 103 were discussed. Applicants' representatives discussed various features of the present invention, including the surprising ability of the yeast vehicle element of the invention to induce dendritic cell (DC) maturation and to significantly enhance the ability of the DCs to present antigen, *regardless* of whether an antigen provided with the yeast vehicle is expressed by the yeast (*e.g.*, recombinantly) *or* provided exogenously to the DC (not expressed by the yeast or carried intracellularly by the yeast). In addition, draft claims that focus on the embodiment of the invention where the antigen is not expressed or carried intracellularly by the yeast vehicle were presented and discussed. The Examiner indicated that claims directed to this embodiment of the invention may overcome his rejections under 35 U.S.C. § 103, and language to clarify this embodiment in the new claims was discussed.

Claim Amendments

All prior claims have been cancelled, without prejudice to or disclaimer of the subject matter therein. New Claims 34-49 have been added.

Support for Claim 34 (and Claim 46) is found in original and prior Claim 1 (supported as previously discussed), and in the specification on page 12, lines 34-35; page 28, lines 33-35; and page 29, line 9-10.

Claims 35-38 are similar to prior dependent Claims 9-12, respectively.

Claims 39-41 are similar to prior dependent Claims 31-33, respectively.

Claims 42 and 43 are similar to prior dependent Claims 13 and 14, respectively.

Claim 44 is similar to prior method Claim 16 (subject to rejoinder), but has been amended to be commensurate in scope with the product of Claim 1.

Claim 45 is similar to prior dependent Claim 22.

Claims 47 and 50 are similar to prior method Claim 23 (subject to rejoinder), but have been amended to be commensurate in scope with the product of Claim 1.

Claims 48 and 49 are similar to prior dependent Claims 24 and 25, respectively.

Claim Objection

The Examiner's objection to Claim 15 is moot in view of the cancellation of this claim.

Rejection of Claims 1-3, 8, 9, 11-15, 29 and 31-33 Under 35 U.S.C. § 103:

The Examiner has rejected Claims 1-3, 8, 9, 11-15, 29 and 31-33 under 35 U.S.C. § 103, contending that these claims are not patentable over Barbera-Guillem and Paglia et al. in view of Duke et al. Specifically, the Examiner asserts that the teachings of Duke et al. provide motivation to use the yeast vehicles disclosed therein as a means of delivery of the antigens to a DC, and therefore is an alternative to the methods of Barbera-Guillem and Paglia et al. The Examiner contends that Duke et al. teaches that yeast vehicles may be used to contact a population of cells and that such cells may be administered to an animal to induce an immune response. The Examiner further contends that Duke et al. teach that the yeast vehicles permit both humoral and cellular immune responses and avoid the need for an adjuvant. The Examiner finally contends that it is not clear that those of skill in the art would have found it surprising that the claimed DCs would be more effective than those stimulated only with pulsed antigens.

Initially, it is submitted that the rejection of Claims 1-3, 8, 9, 11-15, 29 and 31-33 under 35 U.S.C. § 103 is moot, due to the cancellation of these claims. However, to expedite prosecution in view of the newly presented claims, Applicants submit that the combination of Duke et al., Barbera-Guillem et al. and Paglia et al. do not teach or suggest the presently claimed invention. First, none of the references, alone or in combination, teach or suggest the intracellular loading of DCs with a yeast vehicle and a heterologous immunogen, wherein the immunogen is not expressed by or loaded into the yeast vehicle prior to loading into the DC. With regard to the use of the term "immunogen" in the claims, it is noted that the terms "antigen" and "immunogen" can be used interchangeably, as

set forth on page 12 of the specification, and the term "immunogen" has been selected to convey that the antigen is an antigen against which an immune response is desired. The teachings of Duke et al. are limited to a yeast vehicle that carries an antigen intracellularly, either by transformation with a recombinant nucleic acid molecule encoding an antigen or by loading the yeast intracellularly with an antigen. Barbera-Guillem et al. is directed to the provision of antigens to a DC using antibodies and a target cell (a tumor cell or a virally infected cell against which the immune response is to be generated). Paglia et al. is directed to pulsing GM-CSF-matured DCs with antigen. Therefore, the references, alone or in combination, fail to teach the presently claimed invention.

Furthermore, as discussed in the December 14 interview, the present specification has demonstrated that the loading of a DC with a yeast vehicle and an antigen by any means, including (with reference to the present claims), by providing the antigen *exogenously* to the yeast (*i.e.,* not expressed by or contained within the yeast), causes DCs to mature and significantly enhances the ability of a DC to present antigen via both the class I and the class II pathways, as compared to DCs that are pulsed by antigen alone. This is illustrated in Example 5 and Figs. 3B and 3C, for example, where DCs, when provided with an admixture of yeast (YVEC) and exogenous antigen (OVA) (*i.e.,* the antigen is not expressed by or contained with the yeast), stimulated T cells via Class I or Class II significantly better than DCs provided with the equivalent dose of antigen alone. These results demonstrate that the yeast vehicle does not need to *deliver* the antigen to the DC, and that even when the antigen is not expressed or contained within the yeast, the combination of antigen and yeast have a *significant* impact on the ability of the DC to serve as an antigen presenting cell. These effects on DCs were not taught or suggested by any of the cited references, and was quite surprising. Indeed, the Examiner contends that the cited reference of Duke et al. is an alternative means of *delivering* the antigen to a DC, which Applicants believe illustrates this point. Therefore, it is submitted that the combination of references fails to teach or suggest the presently claimed invention.

In view of the foregoing remarks, the Examiner is respectfully requested to withdraw the rejection of Claims 1-3, 8, 9, 11-15, 29 and 31-33 under 35 U.S.C. § 103.

Rejection of Claims 1-3, 8, 9, and 11-15 Under 35 U.S.C. § 103:

The Examiner has rejected Claims 1-3, 8, 9 and 11-15 under 35 U.S.C. § 103, contending that these claims are not patentable over Duke et al. in view of Tomai. Specifically, the Examiner contends that those in the art would have been motivated to use the methods of Duke et al. as a functional alternative to the methods of activating DCs described by Tomai in view of the teachings of the benefits of the yeast vehicles described therein. The Examiner alleges that the references are complementary, and that the combined teachings render the present invention obvious.

It is submitted that the rejection of Claims 1-3, 8, 9 and 11-15 under 35 U.S.C. § 103 is moot, due to the cancellation of these claims. However, to expedite prosecution in view of the newly presented claims, Applicants submit that the combination of Duke et al. and Tomai do not teach or suggest the presently claimed invention. Applicants refer to the discussion presented above, and submit that for the same reasons, the combination of Duke et al. and Tomai fails to teach or suggest the presently claimed invention. Specifically, the teachings of Duke et al. are limited to a yeast vehicle that carries an antigen intracellularly, either by transformation with a recombinant nucleic acid molecule encoding an antigen or by loading the yeast intracellularly with an antigen. Tomai teaches the use of imidazoquinoline immune response modifying compounds to induce the maturation of dendritic cells *in vitro* and enhance the ability of the DCs to stimulate T cells. The references, alone or in combination, fail to teach or suggest the intracellular loading of DCs with a yeast vehicle and a heterologous immunogen, wherein the immunogen is not expressed by or loaded into the yeast vehicle prior to loading into the DC. Also, for the reasons discussed in the first rejection under § 103 above, the combination of references failed to teach or suggest that the provision of yeast and antigen to DCs in any form, including by providing the antigen exogenously, would have the effects on DCs that have been discovered by the present inventors.

In view of the foregoing remarks, the Examiner is respectfully requested to withdraw the rejection of Claims 1-3, 8, 9 and 11-15 under 35 U.S.C. § 103.

Applicants have attempted to address all of the Examiner's issues as set forth in the June 15 Office Action. Any further questions or concerns regarding the claims or Applicants' position should be directed to the below-named agent at (303) 863-9700.

Respectfully submitted,

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Date: 15 December 2005